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10/073,333	02/13/2002	Kevin P. Baker	PF514P1	4576

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	13

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/073,333	Applicant(s) BAKER ET AL.	
	Examiner Eileen O'Hara	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-23,27 and 29-88* is/are pending in the application.

4a) Of the above claim(s) *10 and 20-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-9, 11-19, 27 and 29-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,5-23,27 and 29-88* ~~are~~ were subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 August 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1, 5-23, 27 and 29-88 are pending in the instant application. Claim 1 has been amended, claims 2-4, 24-26 and 28 have been canceled and claims 29-88 have been added as requested by Applicant in Paper Number 12, filed April 10, 2003.

Election/Restriction

2. Applicant's election with traverse of Group I, and further election with traverse of a nucleic acid comprising a polynucleotide encoding a TR16 protein (SEQ ID NOS: 2 and 4), in Paper No. 12 is acknowledged. The traversal is on the ground(s) that restriction remains improper unless it can be shown that the search and examination of multiple groups would entail a "serious burden." Applicants further point out that the Examiner has classified Groups IV, V and VI in the same class and subclass, so that they have not acquired a separate status in the art, and would not present a serious burden to search and examiner together, and that thus, in view of M.P.E.P. § 803, the claims of all Groups I-VI should be searched and examined together. Applicants submit that a search of the sequence of Group I would provide useful information for the sequences of Group II, and that a search of both of these groups would largely, if not entirely, overlap, and since Groups II and III are directed to amino acid sequences and antibodies they bind, a search of both of these groups would largely, if not entirely, overlap, and therefore the search and examination of all of the groups would not entail a serious burden. This is not found persuasive because consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search:. These criteria were met in the above

restriction. A search for antibodies to a protein would constitute a different search than that of a search for the protein. It is old and well known in the art that antibodies have been generated without having purified protein, and antibodies to one protein may also cross-react with a related protein. Additionally, the nucleic acids, proteins and antibodies are classified separately, and as stated in the MPEP § 803, "a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02.". Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. Though Groups IV-VI are in the same class and subclass, they are in a different class and subclass from the other groups and require separation search and consideration. Also argued is that a search for one group would be overlapping and provide useful information about the other groups. However, the fact that some useful information may be obtained in the searches of one group for that of another group, and the fact that there may possibly be overlaps in the searches is not a sufficient basis for holding the restriction to be improper, because the search and examination of one group may not yield all of the necessary information for the other group. Thus, the groups require divergent searches, and to search all inventions would be burdensome.

Applicant's election with traverse within Group I of a TR16 nucleic acid encoding a polypeptide of SEQ ID NO: 2 or 4 is acknowledged. The traversal on pages 17-19 of the response is on the ground(s) that the Examiner has not disclosed any statutory or regulatory basis for the further restriction within the provisionally elected group I. Applicants note that the Examiner is requiring an election of group members of the Markush-type claim (claim 10), and point out that MPEP § 803.02 requires that if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all claims on the merits. Applicants submit that the members of the Markush groups of the pending claims to provisionally elected group I are sufficiently few in number and very closely related, as they are all different portions of the same TR16 polynucleotide sequence, so that a search of all of the members may be made without a serious burden, and moreover, even assuming that examination of the entire claim would present a serious burden, MPEP § 803.02 states that "[f]ollowing election, the Markush-type claim will be examined fully as to the elected species and further to the extent necessary to determine patentability.", and that if no prior art is found "that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. Applicants also point out that MPEP § 803.04 holds that even when nucleotide sequences encoding different proteins are contained in an application, a reasonable number, normally ten sequences, will be examined in a single application. Applicants submit that the instant nucleic acids encode different fragments of the same proteins rather than different proteins as contemplated by § 803.04, and that section 803.04 further states that "nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together."

Applicants submit that the present requirement for further election within group I is improper, and Applicants further submit that a reasonable number of such nucleic acids should be examined together, and the Examiner has given no indication why ten sequences are unreasonable in the present case.

Applicants' arguments have been fully considered but are not deemed persuasive. The search for more than one product would be burdensome, because due to the use of 'comprising' language, nucleic acids encoding the specific epitope-bearing regions in claim 10 may be found in different nucleic acid sequences. Nucleic acids encoding the specific epitope-bearing regions have unique nucleotide sequences that are different and require separate and non coextensive searches. It cannot even be said that the search for nucleic acids encoding amino acids 1-963 of SEQ ID NO: 2 would reveal art pertaining to, for instance a nucleic acid *comprising* a region encoding amino acids 222-223 of SEQ ID NO: 2, as the latter could be found embedded in a completely different protein. Therefore, each of the specific epitope-bearing regions in claim 10 would require a separate sequence search, and as there are 28 such epitope-bearing regions claimed, this would be a serious burden.

Accordingly, restriction is proper.

As to Applicants' arguments that a reasonable number of sequences, up to ten, should be examined together, the U.S.P.T.O considers a search for more than one nucleic acid sequence and encoded protein a burden because the Office would have to search several different databases for the separate sequences, which would be a serious burden on the examiner and the office, especially considering the enormous numbers of sequences currently deposited in the sequence databases, which is continuing to grow at a logarithmic rate.

The requirement is still deemed proper and is therefore made FINAL.

Claims 10 and 20-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Claims 1, 5-9, 11-19, 27 and 29-88 are currently under examination.

Information Disclosure Statement

3. The sequences disclosed in the IDS filed April 10, 2003 have been considered to the extent that was possible absent an explanation of relevance or a sequence alignment.

Priority Statement in First line of Specification

4. This application filed under former 37 CFR 1.60 lacks the current status of the nonprovisional parent application 09/637,856. A statement reading "(now abandoned)" should be included after "09/637,856, filed August 10, 2000" in the first sentence of the specification.

Specification

The disclosure is objected to because of the following informalities:

5.1 Figure 2 of the instant application are presented on four separate panels, and have been labeled correctly as Figures 2A-D in accordance with 37 C.F.R. § 1.84(U)(1). However, the legend to Figure 2 on page 6 of the specification does not refer to 2A-D. Applicant is required to file an amendment under 37 C.F.R. § 1.312 to change the Brief Description of the Drawings and the rest of the specification accordingly. If, for example, Figure 1 is divided into Figures 1A, 1B

and 1C then the Brief Description and all references to this figure in the specification must refer to Figures 1A, 1B and/or 1C.

5.2 37 C.F.R. §1.821(d) states:

> Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

A sequence disclosed in Figure 4 without the required reference to the sequence identifier (SEQ ID NO:). Also, the instant specification needs to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. This can be resolved by adding a reference to the Figures or the Brief Description of the Drawings. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

Applicants are required to amend the specification to comply with 37 C.F.R. §1.821(d).

5.3 The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Nucleic Acids Encoding Human Tumor Necrosis Factor TR16.

Appropriate correction is required.

Double Patenting

6. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1, 5-9, 11-19, 27 and 29-88 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-19 and 26 of copending Application No. 10/140,164. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1, 5-9, 11-19, 27 and 29-88 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1, 5-9, 11-19, 27 and 29-88 are directed to nucleic acids encoding the proteins of SEQ ID NOS: 2 and 4, identified as TR16 receptor (short form and long form, respectively). The instant specification discloses that the polypeptide of SEQ ID NO: 2 is a 963 amino acid

protein, and the polypeptide of SEQ ID NO: 4 is a 1027 amino acid protein. The proteins of SEQ ID NOS: 2 and 4 are identical from amino acids 1-955, after which the sequences diverge. The specification teaches that the receptor shares the greatest degree of homology with the known tumor necrosis factor receptors human TNFR 1 and OX40, including significant sequence homology over multiple cysteine rich domains, and provide a sequence alignment of SEQ ID NO: 2 with these receptors (Fig. 2). The specification asserts that the TR16 proteins are members of the tumor necrosis factor receptor family due to this structural homology and presence of multiple cysteine residues. Although this structural homology is supportive of this protein being a receptor of the TNFR family, the protein does not have any specific and substantial utility, or a well established utility, as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001.

The instant application states that functional activities of the TR16 polypeptides are biological activity, antigenicity, immunogenicity, ability to form multimers with TR16 polypeptides of the invention. These are general activities that would apply to virtually any protein in the tumor necrosis receptor family, and are not specific to this particular protein. The specification also describes the uses and methods of the invention, in which the proteins and nucleic acids can be used in methods such as screening assays to identify ligands, binding proteins, agonists or antagonists, to raise monoclonal or polyclonal antibodies, use of the nucleic acid to make fusion proteins or to identify chromosomes or location of particular sites on a chromosome, expressing the nucleic acid in order to make the protein, or to determine tissue expression by Northern blotting, for example, or to quantitate or qualitate the concentration of

cells B cell lineage (e.g., B cell leukemia cells) expressing TR16, or to use the TR16 proteins in bioassays to determine the effect of the proteins on various biological activities, such as on stimulated proliferation and/or differentiation on cells, wound healing, or angiogenesis for example, as described in Examples 14-35.

However, none of these uses are considered to be specific or substantial utilities for either the proteins or the encoding nucleic acid molecules. Methods such as identification of ligands, use to screen for homologous genes, use to identify chromosomes or chromosomal location, use to recombinantly produce protein or fusion proteins or use to generate antibodies are considered general methods applicable to any protein and/or nucleic acid, and are not considered specific or substantial. Quantitation or qualitation of B cells is also not a specific or substantial utility, as TR16 is also expressed in many other cell types and tissues and is not specific to B cells. Use of TR16 in bioassays is also not a specific and substantial utility, and is only further research to discover what the activities and biological significance of the proteins are. On page 236, the specification states that TR16 has been mapped to chromosome 7q21, an area in which chromosomal rearrangements have been implicated in lymphomas, and further asserts that relationships between genes and diseases that have been mapped to the same chromosomal region can be identified through linkage analysis. This is not a specific utility as all cDNAs can be mapped to a chromosomal location, and no relationship between TR16 and any specific disease has been disclosed. A correlation between the location or altered sequence of TR16, such as a restriction fragment length polymorphism, and a disease would be a specific and substantial utility for the nucleic acid, but no such correlation has been made.

The instant application also teaches that the protein and nucleic acids, associated

antibodies, agonists, antagonists and antisense nucleic acids can be used either diagnostically to detect abnormal levels of the TR16 protein or nucleic acids, identify mutations, disorders or diseases, or prophylacticly or therapeutically to treat diseases or disorders, such as those listed throughout the specification and especially on pages 135, 187-189, 191-194, 199-207, and include diseases, disorders or infections such as immune system disorders, viral, fungal, parasitic or bacterial infectious disease, graft-host disease, immunodeficiency, autoimmune diseases and the like, cancers, AIDS, neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Retinitis pigmentosa among others, myelodysplastic syndromes such as aplastic anemia, ischemic injury such as caused by stroke or myocardial infarction, toxin-induced liver disease, septic shock, cachexia and anorexia, cardiovascular disorders, cerebrovascular disorders, blood-composition-affecting disorders, or can be used for the expansion of immature hematopoietic progenitor cells and as a modulator or hematopoietic stem cells in vitro for the purpose of bone marrow transplantation and/or gene therapy, to increase the concentration of blood cells in individuals, in erythropoietin therapy, and as a vaccine adjuvant, among others listed.

However, the assertion that the protein and/or nucleic acids of the instant invention can be used in the diagnosis or treatment of diseases or disorders is also not a specific and substantial utility, and is based on both the tissue expression of TR16 and the assumption that the proteins are receptors in the tumor necrosis factor receptor family, which as a family are involved in myriad biological pathways and activities and disorders. Many proteins are members of evolutionarily related families, yet have diverse biological activities and functions. The members of the tumor necrosis receptor family bind distinct ligands and have specific biological

activities. There is no ligand known to bind and activate the TR16 protein, and the biological activities upon ligand binding are also not known for this protein.

There is no nexus between any of the diseases or disorders and the molecules of the instant invention. Given no disease state or any other function or activity known for the protein, the protein is not considered to have utility. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct,.1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to nucleic acids encoding proteins which have undetermined function or biological significance, and the use of orphan receptors to discover their ligands or properties does not constitute a specific, substantial utility. All of the biological activities of a protein need not be known to obtain a patent, but there must be some specific and substantial activity or function disclosed. It is possible that after further characterization, these proteins or encoding nucleic acids might be found to have a patentable utility, such as association with a specific disease. This further characterization, however, is part of the act of invention, and until it has been undertaken the Applicants' claimed invention is incomplete. Because there is no specific and substantial utility asserted, credibility cannot be assessed.

Example 18 on pages 268-269 of the specification discloses an experiment in which TR16 was assayed for inhibition of B cell proliferation in an *in vitro* co-stimulatory assay. However, the assay as written is confusing, and it is not clear what the steps were, what the controls were, and the results obtained. The conclusury statement on page 269 (paragraph 0671) is unclear. Additionally, the statement on page 289, paragraph 0777, appears to be misplaced, and appears to belong to Example 18, and not Example 35, which describes a lymphodema animal model. Paragraph 0777 states that the results of this experiment confirmed that TR16-Fc inhibited B cell proliferation in the co-stimulatory assay, and that other tumor necrosis factor receptor fusion proteins did not. Clarification of this is requested, in order to determine if this activity of TR16 could be a specific and substantial utility. However, until such clarification, there is no specific and substantial utility attributable to the proteins or encoding nucleic acids.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8.1 Claims 1, 5-9, 11-19, 27 and 29-88 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling of how to use the TR16 polypeptide (or nucleic acid), enablement would not be found commensurate in scope with the claims. If one of skill in the art does not know how to use the nucleic acids or proteins the skilled artisan would clearly not know how to use nucleic acid

molecules comprising a polynucleotide having a nucleotide sequence at least 95% identical to a nucleotide sequence encoding polypeptides that are 95% identical to the polypeptides of SEQ ID NO: 2 or 4 or encoding polypeptides comprising the specifically recited domains or epitope-bearing portions thereof.

8.2 Claims 1, 5-9, 11-19, 27 and 62-88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims require the cDNA clones HTWBD48 and HLICS62. Applicants' referral to the deposit of cDNA clones HTWBD48 and HLICS62 on page 5 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State. Additionally, amendment of the specification to recite the date of the deposit, the complete name and address of the depository, and the accession number of the deposited cell line is required.

8.3 Claims 1, 8, 9, 11-19, 27, 29, 30, 33, 36, 39, 42, 45, 48-60, 62, 63, 65, 67, 69, 71, 73 and 75-87 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes the polypeptide sequences consisting of SEQ ID NOS: 2 and 4, which are identical over the first 955 amino acids and which diverge in the intracellular domain. As discussed in the rejection under 35 USC § 101, there is no specific and substantial activity attributable to the proteins or encoding nucleic acids. However, the claims as written include nucleic acid molecules encoding polypeptides comprising fragments and homologues, encompass polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of two polypeptides that are identical over the majority of the length of the proteins, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, only two polypeptides which are identical over most of their length and differ only for part of the intracellular domain. Protein function, however, cannot be reliably predicted from protein sequence homology. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrogenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does allow predictability in this instance. Given the unpredictability of homology

comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences, and the claims encompass a broader genus than the Applicants have defined.

The written description guidelines indicate that a representative species may be adequately described through its structure, through its functional characteristics, or through a combination of its structure and function. There is no functional limitation in the claims, and some of the claims require only a very small amount of structure. For example, claim 10 only requires that the isolated nucleic acid comprises a polynucleotide which encodes the amino acid sequence of an eptiope-bearing portion of the protein of SEQ ID NOS: 2 or 4 or the recited domains thereof, which as defined in the specification may be as few as 4 amino acids.

The instantly claimed genus is not so limited and the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polynucleotides encompassed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 5-9, 11-18 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 5-9, 11-18 and 27 are indefinite because claims 1, 13, and 27 encompass a nucleic acid molecule encoding ***the*** TR16 intracellular domain, and the specification discloses two TR16 polypeptides that have different intracellular domains, so it is not clear which intracellular domain is being claimed. The other claims are rejected for depending from claim 1.

Claim 27 is also indefinite because in part (e), it encompasses a nucleotide sequence encoding the mature TR16 polypeptide having the amino acid sequence encoded by ***the*** cDNA clone contained in ATCC Deposit No. PTA-506, and PTA-506 contains two cDNA clones, HTWBD48 and HLICS62.

Claim 27 is also indefinite because the "at least one" language of the claims does not place an upper limit on the extent of the changes to be made. For example, as written, it may be possible to make conservative amino acid substitutions at every amino acid residue, but the protein would be completely different from those of the recited SEQ ID NOS. Therefore, the claims fail to adequately point out that which Applicant sees as the invention.

Priority

10. 35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional

> application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 or § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, which respect to the now claimed invention. Because the instant application does not meet the requirements of 35 U.S.C. § 112, first paragraph, for those reasons given above and it is a continuation of application Serial Numbers 60/268,364, 09/637,856, 60/148,348, 60/148,683, 60/148,758, 60/148,870, 60/149,181, 60/149,453, 60/149,498, the prior applications do not meet those requirements and, therefore, are unavailable under 35 U.S.C. § 120 or § 119(e). The effective priority date of the instant application is considered to be the filing date of this application, Feb. 13, 2002, because the claimed invention is not supported by either a specific and substantial utility or a well established utility.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11.1 Claims 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Shimkets et al., WO 00/78802, December 28, 2000 (cited by Applicants).

Claims 8 and 9 encompass an isolated nucleic acid molecule comprising a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a sequence identical to a nucleotide sequence encoding the polypeptide sequences of SEQ ID NOS: 2 or 4 (SEQ ID NOS: 1 and 3) or extracellular domains of SEQ ID NOS: 2 or 4, or an isolated nucleic acid molecule comprising a polynucleotide which encodes the amino acid sequence of an epitope bearing portion of a polypeptide of SEQ ID NOS: 2 or 4. Stringent hybridization conditions are defined on page 62 of the specification, and the specification teaches on page 132 that an antigenic epitope-bearing peptides can be 4 amino acids in length.

Shimkets et al. disclose a nucleic acid molecule having a nucleotide sequence (Figure 10) that is 98.7% identical to nucleotides 189-1743 of SEQ ID NO: 1 or 3 and encodes a polypeptide that is 99.6% identical to amino acids 115-565 of SEQ ID NOS: 2 or 4 (part of the extracellular domain, see attached sequence alignments). This nucleic acid molecule would hybridize to a polynucleotide having a sequence identical to a nucleotide sequence encoding the polypeptide sequences of SEQ ID NOS: 2 or 4 under stringent hybridization conditions, and also encodes an epitope-bearing portion of the polypeptides of SEQ ID NOS: 2 and 4. Therefore, Shimkets et al. anticipates the claims.

11.2 Claims 8 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Shimkets et al., US Patent Application Publication No. US20030032095A1, filing date Nov. 2, 2001.

Claims 8 and 9 are described above.

Shimkets et al. disclose a nucleic acid molecule having a nucleotide sequence (SEQ ID NO: 19) that is 98.7% identical to nucleotides 189-1743 of SEQ ID NO: 1 or 3 and encodes a polypeptide that is 99.6% identical to amino acids 115-565 of SEQ ID NOS: 2 or 4 (part of the extracellular domain, see attached sequence alignments). This nucleic acid molecule would hybridize to a polynucleotide having a sequence identical to a nucleotide sequence encoding the polypeptide sequences of SEQ ID NOS: 2 or 4 under stringent hybridization conditions, and also encodes an epitope-bearing portion of the polypeptides of SEQ ID NOS: 2 and 4. Therefore, Shimkets et al. anticipates the claims.

11.3 Claims 8 and 9 are rejected under 35 U.S.C. 102(a) as being anticipated by Tashiro et al., EMBL/GenBank/DDBJ databases, Accession No. AK055902, December 1, 2001.

Claims 8 and 9 are described above.

Tashiro et al. disclose a nucleic acid molecule having a nucleotide sequence that is 93.2% identical to nucleotides 504-3373 of SEQ ID NO: 1 and 98.6% identical to nucleotides 504-3539 of SEQ ID NO: 3 and encodes a polypeptide that is 100% identical to amino acids 334-675 of SEQ ID NOS: 2 or 4 (part of the extracellular domain, see attached sequence alignments). This nucleic acid molecule would hybridize to a polynucleotide having a sequence identical to a nucleotide sequence encoding the polypeptide sequences of SEQ ID NOS: 2 or 4 under stringent hybridization conditions, and also encodes an epitope-bearing portion of the polypeptides of SEQ ID NOS: 2 and 4. Therefore, Tashiro et al. anticipates the claims.

11.4 Claims 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Hedge et al., et al., Database EST, Accession No. AW954806, June 1, 2000.

Claims 8 and 9 are described above.

Hedge et al. disclose a nucleic acid molecule having a nucleotide sequence that is 98.8% identical to nucleotides 1440-2081 of SEQ ID NOS: 1 and 3. This nucleic acid molecule would hybridize to a polynucleotide having a sequence identical to a nucleotide sequence encoding the polypeptide sequences of SEQ ID NOS: 2 or 4 under stringent hybridization conditions, and also encodes an epitope-bearing portion of the polypeptides of SEQ ID NOS: 2 and 4 (approximately amino acids 480-664 of SEQ ID NOS: 2 and 4). Therefore, Hedge et al. anticipates the claims.

11.5 Claims 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Bevins et al., US Patent No. 5,641,497.

Claim 9 encompasses an isolated nucleic acid molecule comprising a polynucleotide which encodes the amino acid sequence of an epitope bearing portion of a polypeptide of SEQ ID NOS: 2 or 4.

Bevins et al. disclose a polypeptide (SEQ ID NO: 7) that is identical over eight amino acids (amino acids 8-15) to amino acids 936-943 of SEQ ID NOS: 2 or 4 of the instant application, and nucleic acid molecule (SEQ ID NO: 6) that encodes this portion (nucleotides 40-63 of SEQ ID NO: 6). Since an epitope-bearing portion may be at least four amino acids, the nucleic acid molecule of Bevins et al. anticipates the claim.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

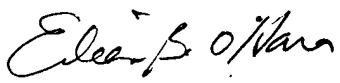
Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.



Patent Examiner